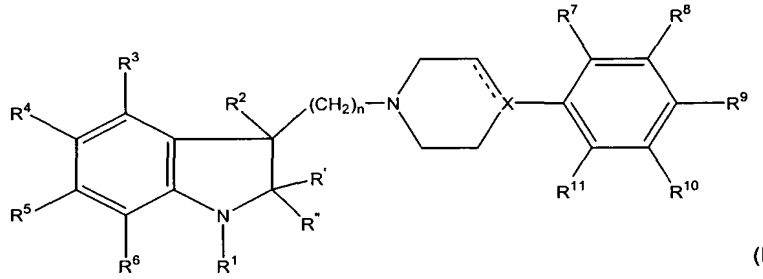
Claims

1. A method of treating the positive and negative symptoms of schizophrenia, other psychoses, anxiety disorders, depression, aggression, side effects induced by conventional anti-psychotic agents, migraine, cognitive disorders, dyskinesia induced by treatment with L-dopa, attention deficit hyperactivity disorder and improving sleep quality, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of formula (I)



(I)

wherein R^1 is acyl, thioacyl, trifluoromethylsulfonyl, or R^1 is a group $R^{12}SO_2$-, $R^{12}OCO$- or $R^{12}SCO$- wherein R^{12} is C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl or aryl, or R^1 is a group $R^{13}R^{14}NCO$, $R^{13}R^{14}NCS$-, wherein R^{13} and R^{14} are independently hydrogen, C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl or aryl, or R^{13} and R^{14} together with the N-atom to which they are linked form a pyrrolidinyl, piperidinyl or perhydroazepin group;

n is 1-6;

X is C, CH or N, and the dotted line emanating from X indicates a bond when X is C and no bond when X is N or CH;

R', R'' and R^2 are independently selected from hydrogen and C_{1-6}-alkyl optionally substituted with halogen; and

R^3-R^{11} are independently selected from hydrogen, halogen, cyano, nitro, C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, amino, C_{1-6}-alkylamino, di-(C_{1-6}-alkyl)amino, C_{1-6}-alkylcarbonyl, aminocarbonyl, C_{1-6}-alkylaminocarbonyl, di-(C_{1-6}-alkyl)aminocarbonyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, trifluoromethyl, trifluoromethylsulfonyl and C_{1-6}-alkylsulfonyl; or a pharmaceutically acceptable acid addition salt thereof.

2. The method of claim 1, wherein the anxiety disorders are selected from the group consistng of generalized anxiety disorder, panic disorder and obsessive compulsive disorder.

3. The method of claim 1, wherein the compound of formula (I) is in the form of the S-enantiomer.

4. The method of claim 1 or 3 wherein R^7 and R^{11} are hydrogen.

5. The method of claim 4 wherein R^{10} is hydrogen.

6. The method of claim 1 wherein X is CH and the dotted line indicates a bond.

7. The method of claim 1 wherein at least one of R^8 and R^9 are independently selected from halogen, cyano, nitro, C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, amino, C_{1-6}-alkylamino, di-(C_{1-6}-alkyl)amino, C_{1-6}-alkylcarbonyl, aminocarbonyl, C_{1-6}-alkylaminocarbonyl, di-(C_{1-6}-alkyl)aminocarbonyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, trifluoromethyl, trifluoromethylsulfonyl and C_{1-6}-alkylsulfonyl.

8. The method of claim 1 wherein n is 2 or 3.

9. The method of claim 8 wherein n is 2.

10. The method of claim 1 wherein R^1 is acyl.

11. The method of claim 10 wherein R^1 is acetyl.

12. The method of claim 1 wherein R^4 is hydrogen or fluoro.

13. The method of claim 1 wherein the compound of formula (I) is selected from the group consisting of

(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(3,4-dimethylphenyl)piperazine;

(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(4-methylphenyl)piperazine;

(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(4-methylphenyl)piperidine;

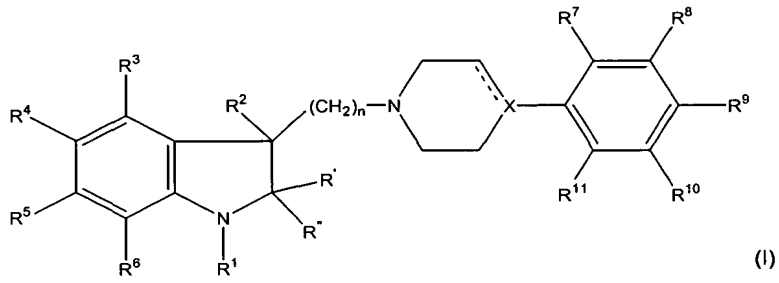
(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(3,4-dichlorophenyl)piperazine;

(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(4-bromophenyl)piperazine;

1-[2-(1-Acetyl-2,3-dihydro-1H-indol-3-yl)ethyl]-4-(3,4-dichlorophenyl)-3,6-dihydro-2H-pyridine; and 1-[2-(1-Acetyl-2,3-dihydro-1H-indol-3-yl)ethyl]-4-(3,4-dichlorophenyl)piperidine;

or a pharmaceutically acceptable salt thereof.

14. A 3-indoline derivative of formula (I)



(I)

wherein R^1 is acyl, thioacyl, trifluoromethylsulfonyl, or R^1 is a group $R^{12}SO_2$, $R^{12}OCO$- or $R^{12}SCO$- wherein R^{12} is C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl or aryl, or R^1 is a group $R^{13}R^{14}NCO$, $R^{13}R^{14}NCS$-, wherein R^{13} and R^{14} are independently hydrogen, C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl or aryl, or R^{13} and R^{14} together with the N-atom to which they are linked form a pyrrolidinyl, piperidinyl or perhydroazepin group; and

n is 1-6;

X is C, CH or N, and the dotted line emanating from X indicates a bond when X is C and no bond when X is N or CH;

R', R'' and R^2 are independently selected from hydrogen and C_{1-6}-alkyl optionally substituted with halogen;

R^3-R^{11} are independently selected from hydrogen, halogen, cyano, nitro, C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, amino, C_{1-6}-alkylamino, di-(C_{1-6}-alkyl)amino, C_{1-6}-alkylcarbonyl, aminocarbonyl, C_{1-6}-alkylaminocarbonyl, di-(C_{1-6}-alkyl)aminocarbonyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, trifluoromethyl, trifluoromethylsulfonyl and C_{1-6}-alkylsulfonyl;

with the proviso that

(i) R^9 may not be hydrogen when R', R'', R^2-R^8, R^{10}-R^{11} are hydrogen, n is 2 and R^1 is acetyl;

(ii) R^9 may not be CF_3 or chloro, when R', R'', R^2-R^8, R^{10}-R^{11} are hydrogen, X is C or CH, n is 2 and R^1 is acetyl;

(i) R^7 or R^{11} may not be methoxy when X is N, n is 2 or 4 and R^1 is acetyl; and

(iv) R^4 may not be methoxy;

or a pharmaceutically acceptable acid addition salt thereof.

15. A compound of claim 14 which is in the form of the S-enantiomer.

16. A compound of claim 14 or 15 wherein R^7 and R^{11} are hydrogen.

17. A compound of claim 16 wherein R^{10} is hydrogen.

18. A compound of claim 14 wherein X is CH and the dotted line is a bond.

19. A compound of claim 14 wherein at least one of R^8 and R^9 are selected from halogen, cyano, nitro, C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, amino, C_{1-6}-alkylamino, di-(C_{1-6}-alkyl)amino, C_{1-6}-alkylcarbonyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, trifluoromethyl, trifluoromethylsulfonyl and C_{1-6}-alkylsulfonyl.

20. A compound of claim 14 wherein n is 2 or 3.

21. A compound of claim 20 wherein n is 2.

22. A compound of claim 14 wherein R^1 is acyl.

23. A compound of claim 22 wherein R^1 is acetyl.

24. A compound of claim 14 wherein R^4 is hydrogen or fluoro and R', R'', R^2, R^3, R^5 and R^6 are hydrogen.

25. A compound of claim 14 which is selected from
(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(3,4-dimethylphenyl)piperazine;

(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(4-methylphenyl)piperazine;
(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(4-methylphenyl)piperidine;
(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(3,4-dichlorophenyl)piperazine;
(+)-1-[2-(1-Acetyl-2,3-dihydro-*1H*-indol-3-yl)ethyl]-4-(4-bromophenyl)piperazine;
1-[2-(1-Acetyl-2,3-dihydro-1H-indol-3-yl)ethyl]-4-(3,4-dichlorophenyl)-3,6-dihydro-2H-pyridine,
and 1-[2-(1-Acetyl-2,3-dihydro-1H-indol-3-yl)ethyl]-4-(3,4-dichlorophenyl)piperidine;
or a pharmaceutically acceptable salt thereof.

26. A pharmaceutical composition comprising compound of claim 14 in a therapeutically effective amount together with one or more pharmaceutically acceptable carriers or diluents.

27. A method of treating the positive and negative symptoms of schizophrenia, other psychoses, anxiety disorders, depression, aggression, side effects induced by conventional anti-psychotic agents, migraine, cognitive disorders, dyskinesia induced by treatment with L-dopa, attention deficit hyperactivity disorder and in the improvement of sleep quality, comprising administration of a therapeutically effective amount of a compound of claim 14.

28. The method of claim 27, wherein the anxiety disorders are selected from the group consisting of generalized anxiety disorder, panic disorder and obsessive compulsive disorder.